

Serial No. 09/868,974

Amendments to the Claims

1-26. (Cancelled)

27. (new) A shelf-stable solution formulation comprising a therapeutically effective amount of a glucagon-like peptide-1 (GLP-1) molecule which comprises the amino acid sequence:

R<sub>1</sub>-X-Glu-Gly<sup>10</sup>-Thr-Phe-Thr-Ser-Asp<sup>15</sup>-Val-Ser-Ser-Tyr-  
Leu<sup>20</sup>-Y-Gly-Gln-Ala-Ala<sup>25</sup>-Lys-Z-Phe-Ile-Ala<sup>30</sup>-Trp-Leu-Val-  
Lys-Gly<sup>35</sup>-Arg-R<sub>2</sub> (SEQ ID NO:2)

wherein R<sub>1</sub> is His or desamino-histidine, X is Ala, Gly or Val, Y is Glu or Gln, Z is Glu or Gln and R<sub>2</sub> is Gly-OH, and further comprising one additional amino acid substitution;

a pharmaceutically acceptable preservative; and a tonicity modifier, wherein said formulation has a pH that is about 8.2 to about 8.8.

28. (new) The formulation of claim 27 wherein the formulation has a pH that is about 8.2 to about 8.5.
29. (new) The formulation of claim 27, wherein R<sub>1</sub> is L-histidine, X is Val, Y is Glu, Z is Glu, and R<sub>2</sub> is Gly-OH.
30. (new) The formulation of claim 27 wherein the formulation is buffered by Tris.
31. (new) The formulation of claim 30 further comprising a surfactant.
32. (new) The formulation of claim 31 wherein the surfactant is Brij-35.
33. (new) A method for treating diabetes comprising administering to a patient in need of such treatment an effective amount of the formulation of claim 27.
34. (new) A shelf-stable solution formulation comprising a therapeutically effective amount of a glucagon-like peptide-1 (GLP-1) molecule selected from the group consisting of GLP-1(7-34), GLP-1(7-35), GLP-1(7-36), GLP-1(7-

Serial No. 09/868,974

37), or the amide forms thereof, comprising at least one modification selected from the group consisting of:

- (a) substitution of a glycine, serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, phenylalanine, arginine, or D-lysine for lysine at position 26 and/or position 34 or substitution of a glycine, serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, phenylalanine, lysine, or a D-arginine for arginine at position 36;
- (b) substitution of an oxidation-resistant amino acid for tryptophan at position 31;
- (c) substitution of at least one of: tyrosine for valine at position 16; lysine for serine at position 18; aspartic acid for glutamic acid at position 21; serine for glycine at position 22; arginine for glutamine at position 23; arginine for alanine at position 24; and glutamine for lysine at position 26; and
- (d) substitution comprising at least one of: glycine, serine, or cysteine for alanine at position 8; aspartic acid, glycine, serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, or phenylalanine for glutamic acid at position 9; serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, or phenylalanine for glycine at position 10; and glutamic acid for aspartic acid at position 15;

a pharmaceutically acceptable preservative; and a tonicity modifier, wherein said formulation has a pH that is about 8.2 to about 8.8..

- 35. (new). The formulation of claim 34 wherein the formulation has a pH that is about 8.2 to about 8.5.
- 36. (new) The formulation of claim 34, wherein the GLP-1 molecule is selected from the group consisting of GLP-1(7-34), GLP-1(7-35), GLP-1(7-36), GLP-

Serial No. 09/868,974

1(7-37), or the amide forms thereof, and provided that arginine is substituted for lysine at position 34

37. (new) The formulation of claim 34 wherein the formulation is buffered by Tris.
38. (new) The formulation of claim 37 further comprising a surfactant
39. (new) The formulation of claim 38 wherein the surfactant is Brij-35.
40. (new) A method for treating diabetes comprising administering to a patient in need of such treatment an effective amount of the formulation of claim 34.
41. (new) A shelf-stable solution formulation comprising a therapeutically effective amount of a glucagon-like peptide-1 (GLP-1) molecule which comprises the amino acid sequence:
- $R_1$ -X-Glu-Gly<sup>10</sup>-Thr-Phe-Thr-Ser-Asp<sup>15</sup>-Val-Ser-Ser-Tyr-Leu<sup>20</sup>-Y-Gly-Gln-Ala-Ala<sup>25</sup>-Lys-Z-Phe-Ile-Ala<sup>30</sup>-Trp-Leu-Val-Lys-Gly<sup>35</sup>-Arg-R<sub>2</sub> (SEQ ID NO:2)
- wherein R<sub>1</sub> is His or desamino-histidine, X is Ala, Gly or Val, Y is Glu or Gln, Z is Glu or Gln and R<sub>2</sub> is Gly-OH;
- a pharmaceutically acceptable preservative; and a tonicity modifier, wherein said formulation has a pH that is about 8.2 to about 8.8.
42. (new) The formulation of claim 41 wherein the formulation has a pH that is about 8.2 to about 8.5.
43. (new) The formulation of claim 41, wherein R<sub>1</sub> is L-histidine, X is Val, Y is Glu, Z is Glu, and R<sub>2</sub> is Gly-OH.
44. (new) The formulation of claim 41 wherein the formulation is buffered by Tris.
45. (new) The formulation of claim 44 further comprising a surfactant.
46. (new) The formulation of claim 45 wherein the surfactant is Brij-35.

Serial No. 09/868,974

47. (new) A method for treating diabetes comprising administering to a patient in need of such treatment an effective amount of the formulation of claim 41.